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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/511,987	10/21/2004	Judith Aronhime	1662/58602	8819
26646	7590	12/07/2007		
KENYON & KENYON LLP ONE BROADWAY NEW YORK, NY 10004			EXAMINER LAO, MARIALOUISA	
			ART UNIT 1621	PAPER NUMBER
			MAIL DATE 12/07/2007	DELIVERY MODE PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

**Office Action Summary**

Application No.

10/511,987

Applicant(s)

ARONHIME ET AL.

Examiner

M. Louisa Lao

Art Unit

1621

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 15 October 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1,2,5-7 and 10-26 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1,2,5-7 and 10-26 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO/SB/08)  
Paper No(s)/Mail Date 04/17/2007.
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date, \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_.

## **DETAILED ACTION**

### ***Continued Examination Under 37 CFR 1.114***

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10/15/07 has been entered.

### ***Claim Objections***

2. Claim 25 is objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim should refer to other claims in the alternative only, and/or, cannot depend from any other multiple dependent claim. See MPEP § 608.01(n). However, in the furtherance of examining this case, claim 25, including claim 26, which is dependent thereto, have been treated on the merits.

### ***Claim Rejections - 35 USC § 103***

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
  2. Ascertaining the differences between the prior art and the claims at issue.
  3. Resolving the level of ordinary skill in the pertinent art.
  4. Considering objective evidence present in the application indicating obviousness or nonobviousness.
4. The rejection of claims 1, 2, 5-7 and 10-15 is maintained under 35 U.S.C. 103(a) as obvious over Hiskett et al. (USPat 5,861,179, US'179).
5. The instant claims are drawn to a plurality of lamotrigene particles having a specific surface area of from about two to three and a half square meters per gram, wherein the diameter of all the lamotrigene particles in the plurality is equal to or less than 50 $\mu$ m.
6. US'179 in col1 lines 13-67, col2 lines 1-67, col3 lines 22-29 and col3 lines 58-60, teaches the powder formulations of lamotrigene with average particle sizes below 125 $\mu$ m. In col1 lines 5-10, US'179 teaches the pharmaceutical compound lamotrigene; the pharmaceutical formulation of lamotrigene and pharmaceutically acceptable acid addition salts thereof.
7. US'179 teaches the pharmaceutical composition of lamotrigene powder formulations of lamotrigene with average particle sizes below 125 $\mu$ m as well as solid oral dosage form. See Examples.
8. US'179 teaches the use of the lamotrigene in column 1, lines 9-13.
9. US'179 is silent on a plurality of lamotrigene particles having a specific surface area as recited on the instant claims 1, 2, 6 and 7. However, a compound and its properties are inseparable. In re Papesch, 315 F.2d 381, 137 USPQ 43 (CCPA 1963). Since there is a relationship between particle diameter and specific surface area, reduced particle size inherently leads to increased surface area, an artisan with ordinary skill in the art at the time of the invention would know and is logically motivated to apply known particle size reduction

techniques as these are well known optimization steps both in the art and as taught by the prior art with a reasonable expectation that these efforts will attain the desired particle and/or granular size as in the instant claimed application. And the artisan of ordinary skill in the art would know that the reduced size would logically parlay to an increased specific surface area.

10. It is *prima facie* case obvious to combine the teachings of US'179 with the well established relationship between specific surface area and average particle diameter in order to achieve the characteristics of the plurality of lamotrigene particles. Further, one of ordinary skill in the art would have been motivated to optimize the particle size of the lamotrigene particles because the optimization step is considered well in the competence level of an ordinary skilled artisan in the pharmaceutical science, involving merely routine skill in the art. Furthermore, it is within the skill in the art to select optimal parameters, such as amount of ingredients, granular size and specific surface area, in a composition in order to achieve a beneficial effect of increased dissolution.

11. Thus the claimed invention as a whole is clearly *prima facie* obvious over US '179.

12. The rejection of claims 1, 2, 5-7 and 10-26 is maintained under 35 U.S.C. 103(a) as being unpatentable over Hisket et al. (US Pat 5,861,179) as applicable to claims 1, 2, 5-7 and 10-15 above, and further in view of Sawyer et al. (US Pat. 4,602,017, US'017).

13. The instant claims are drawn to a plurality of lamotrigene particles having a specific surface area of from about two to three and a half square meters per gram, wherein the diameter of all the lamotrigene particles in the plurality is equal to or less than 50 $\mu$ m.

14. In col1 lines 13-67, col2 lines 1-67, col3 lines 22-29 and col3 lines 58-60, US'179 teaches the powder formulations of lamotrigene with average particle sizes below 125 $\mu$ m. In

col1 lines 5-10, US`179 teaches the pharmaceutical compound lamotrigene, the pharmaceutical formulation of lamotrigene and pharmaceutically acceptable acid addition salts thereof in solid form. US`017 teaches the use of compounds of the general formula (III), which embraces lamotrigene, for the treatment of CNS disorders. Further, US`017 teaches the use of said compounds in pharmaceutical formulations which can be administered in liquid or solid form (column 3, lines 18-68 through column 4, lines 1-31).

15. It would have been obvious for one skilled in the art to apply the teachings of US`017 for liquid formulations to the US`179's solid pharmaceutical formulation of lamotrigene in order to arrive to the claimed liquid oral dosages of claims 16-24.

16. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. The prior art is indicative of the level of the art, which show that optimization techniques to achieve desired particle sizes and the pharmaceutical compound - lamotrigene, its pharmaceutical compositions and its use are well known in the art.

### ***Response to Arguments***

17. Applicant's arguments filed 10/15/07 have been fully considered but they are not persuasive.

18. Examiner acknowledges the Applicants' arguments on the particle size of the lamotrigine particles stated by cited reference US`179 in the Office Action mailed 10/15/07. However, as the Applicants have quoted in their reply of 3/5/07, the appropriate lines thereto, it is apparent that the particles of US`179, which have a typical size of <125µm read on the particle size of the instant claims of 50µm.

19. Applicants' arguments in the reply filed 10/15/07 focuses on *prima facie obviousness*, particularly a lack of suggestion of the US'179 to use the recited 50 $\mu$ m. Applicants recount the teachings of US'179 to optimize all other parameters, rather than the particle size of lamotrigene.
20. While Applicants emphasize that optimization is not suggested in the cited prior art references, Applicants must have misread that size of <125 $\mu$ m does include sizes of 50 $\mu$ m.
21. Moreover, Applicants must have missed the basis presented in the Office Action dated 9/5/06.

US'179 is silent on a plurality of lamotrigene particles having a specific surface area as recited on the instant claims 1, 2, 6 and 7. However, a compound and its properties are inseparable. In re Papesch, 315 F.2d 381, 137 USPQ 43 (CCPA 1963). Since there is a relationship between particle diameter and specific surface area, reduced particle size inherently leads to increased surface area, an artisan with ordinary skill in the art at the time of the invention would know and is logically motivated to apply known particle size reduction techniques as these are well known optimization steps both in the art and as taught by the prior art with a reasonable expectation that these efforts will attain the desired particle and/or granular size as in the instant claimed application. And the artisan of ordinary skill in the art would know that the reduced size would logically parlay to an increased specific surface area.

And

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. The prior art is indicative of the level of the art, which show that optimization techniques to achieve desired particle sizes and the pharmaceutical compound - lamotrigene, its pharmaceutical compositions and its use are well known in the art.

22. Prior art, like US 2002/0119200, US'200, teaches in page 1 [003-005] that several factors influence drug dissolution, including surface area of the drug. US'200 teaches that it is well known that one way to improve dissolution of drugs is to reduce drug particle size, thus increasing the specific surface area of the drug. US'200 teaches that the smaller the drug particle size, the greater is the advantage in speed of onset of therapeutic effect, or other pharmacodynamic benefit, obtained upon oral administration.

Further, the Supreme Court in *KSR* noted that if the actual application of the technique would have been beyond the skill of one of ordinary skill in the art, then the resulting invention would not have been obvious because one of ordinary skill could not have been expected to achieve it.

23. Further, absent a showing of unexpected results, the cited prior art references render the instant claims obvious.

24. Hence, in light of the non-persuasiveness of the arguments presented, the rejection under 35 USC § 103 of the claims, as amended is **maintained**.

25. **THIS ACTION IS MADE FINAL.**

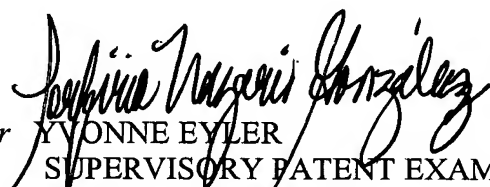
Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136 (a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

### *Correspondence*

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MLouisa Lao whose telephone number is 571-272-9930. The examiner can normally be reached on Mondays to Thursdays from 8:00am to 8:00pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on 571-272-0871. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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